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**Chancellor et al.**

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(54) **SOFT TISSUE AND BONE AUGMENTATION AND BULKING UTILIZING MUSCLE-DERIVED PROGENITOR CELLS, COMPOSITIONS AND TREATMENTS THEREOF**

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#### **U.S. Cl.**

CPC ..... **C12N 5/0659** (2013.01); **A61K 35/34** (2013.01); **C12N 5/0658** (2013.01); **A61K 35/12** (2013.01); **C12N 2500/84** (2013.01); **C12N 2501/70** (2013.01); **C12N 2510/00** (2013.01); **C12N 2533/54** (2013.01)

#### **Field of Classification Search**

CPC ..... **A61K 35/12**; **A61K 35/34**; **C12N 5/0658**; **C12N 5/0659**

USPC ..... 424/93.1; 435/325, 366  
See application file for complete search history.

#### **References Cited**

##### **U.S. PATENT DOCUMENTS**

4,424,208 A 1/1984 Wallace et al.  
4,965,353 A 10/1990 della Valle et al.  
5,053,050 A 10/1991 Itay  
5,130,141 A 7/1992 Law et al.

5,206,028 A 4/1993 Li  
5,336,263 A 8/1994 Ersek et al.  
5,516,532 A 5/1996 Atala et al.  
5,538,722 A 7/1996 Blau et al.  
5,594,032 A 1/1997 Gonzalez-Cadavid et al.  
5,656,478 A 8/1997 Tanagho et al.  
5,667,778 A 9/1997 Atala  
5,833,978 A 11/1998 Tremblay  
5,858,351 A 1/1999 Podsakoff et al.  
5,858,390 A 1/1999 Boss, Jr.  
5,869,041 A 2/1999 Vandenberg  
5,876,447 A 3/1999 Arnett  
5,895,745 A 4/1999 Chandler et al.  
6,001,654 A 12/1999 Anderson et al.  
6,099,832 A 8/2000 Mickle et al.

(Continued)

##### **FOREIGN PATENT DOCUMENTS**

AU 3775799 A 11/1999  
AU 5159901 A 10/2001

(Continued)

##### **OTHER PUBLICATIONS**

Ewton et al, J. Endocrinol. 144(3):539-553, 1995; abstract only.\*  
Acsadi et al. "A Differential Efficiency of Adenovirus-Mediated in vivo Gene Transfer into Skeletal Muscle Cells of Different Maturity." *Hum. Mol. Genet.* 3.4(1994):579-584.  
Adachi et al. "Muscle Derived, Cell Based Ex Vivo Gene Therapy for Treatment of Full Thickness Articular Cartilage Defects." *J. Rheumatol.* 29.9(2002):1920-1930.  
Alden et al. (1999), "In Vivo Endochondral Bone Formation Using a Bone Morphogenetic Protein 2 Adenoviral Vector", *Hum. Gene Ther.*, 10:2245-2253.  
Anderson (1998), "Human gene therapy", *Nature*, 392:25-30.  
Andersson et al. "Advances in the Pharmacological Control of the Bladder." *Exp. Physiol.* 84(1999):195-213.

(Continued)

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#### **(57) ABSTRACT**

The present invention provides muscle-derived progenitor cells that show long-term survival following transplantation into body tissues and which can augment soft tissue following introduction (e.g. via injection, transplantation, or implantation) into a site of soft tissue. Also provided are methods of isolating muscle-derived progenitor cells, and methods of genetically modifying the cells for gene transfer therapy. The invention further provides methods of using compositions comprising muscle-derived progenitor cells for the augmentation and bulking of mammalian, including human, soft tissues in the treatment of various cosmetic or functional conditions, including malformation, injury, weakness, disease, or dysfunction. In particular, the present invention provides treatments and amelioration for dermatological conditions, gastroesophageal reflux, vesico-ureteral reflux, urinary incontinence, fecal incontinence, heart failure, and myocardial infarction.

**10 Claims, 16 Drawing Sheets**  
**(16 of 16 Drawing Sheet(s) Filed in Color)**